A newborn with Factor V Leiden mutation and renal vein thrombosis

Perrone B, Zambelloni C, Motta M, Chirico G
Department of Neonatology and Neonatal Intensive Care, Children’s Hospital, Spedali Civili, Brescia, Italy

Abstract
Authors describe the case of a male term newborn with perinatal left renal vein thrombosis. They underline the central diagnostic role played by the ultrasound scan associated with color and flow-Doppler and the strong association with the inherited thrombophilic status of Factor V Leiden G1691 mutation. They also discuss the utility of anticoagulant therapy.

Keywords: thrombosis, newborn, kidney, ultrasound scan

Introduction
Renal vein thrombosis (RVT) is the most common non-catheter-related thrombotic event during the neonatal period. Acquired and inherited prothrombotic risk factors have to be searched.

Case report
A male neonate born at 39 weeks of gestation by iterative cesarean delivery after a physiological pregnancy (Apgar score 1': 9, 5': 10) with a birth weight of 3860 grams presented, in his second day of life, bile vomit and gross haematuria. The abdominal ultrasound scan showed a globular left kidney enlargement (longitudinal diameter >5 cm), with widespread parenchimal hyperecogenicity and loss of cortico-medullary differentiation (Fig.1). A haemorrhage of the omolateral adrenal gland was associated (Fig.2).

Fig.1 The abdominal ultrasound scan showed a globular left kidney enlargement (longitudinal diameter >5 cm), with widespread parenchimal hyperecogenicity and loss of cortico-medullary differentiation.

Fig.2 Associated haemorrhage of the omolateral adrenal gland

The colour-Doppler examination revealed a severe reduction of the intraparenchimal vascular signal and an absent signal in the left main renal vein. Magnetic resonance (MR) confirmed the diagnosis of complete renal vein thrombosis extending into the inferior caval vein for 5 mm.

Blood count, liver and kidney functions were within normal ranges; thrombophilic screening showed homozygous of Factor V Leiden G1691 mutation.

Anticoagulant treatment was administered with low weight molecular heparin (LWMH) at the term neonates recommended dose (1.7 mg/Kg twice a day) 1, in order to obtain a therapeutic value of anti-Xa activity (0.7-1.2 U/ml). Repeated abdominal ultrasound scans with colour-Doppler study were carried out over the next days and they revealed a gradual improvement of the intraparenchimal perfusion and appearance of prominent hypoechoic pyramids and patchy echogenicity of the renal cortex. Some little calcifications were detected. MR performed on the fifteenth day of life showed partial recanalization of the left main renal vein and disappearance of the thrombotic part extending into the inferior caval vein lumen. Renal function was always normal; transient arterial hypertension regressed spontaneously in a few days. Enoxaparina was administered for 3 months, without adverse effects. During echographic follow up, a progressive hypotrophy of the left kidney was detected and at the third month of life Dimercaptosuccinic acid (DMSA) -scanning showed severe reduction of the left renal function, accounting for 11% of the total function.

Discussion
RVT is the most common non-catheter-related thrombotic event during the neonatal period, accounting for 16-20% of all neonatal thromboembolic events2, 3 with an estimated incidence of 2.2 per 100000 live births.4 Usually symptoms appear early in the
In the majority of cases, after an apparent recovery from the acute phase, the evolution subcapsular renal fluid collections, prominent hypoechoic pyramids, patchy echogenicity to be a severely decreased renal perfusion on color Doppler at the diagnosis, association with poor renal outcome; other features associated with renal atrophy seem as also demonstrated by Winyard et al.7, presenting renal length has a significant effect of long-term outcome on color Doppler ultrasonography. MR is useful to detect the exact thrombus mass, haematuria and thrombocytopenia, is present in no more than 22% of RVT, suggesting that the presence of only one sign is sufficient to suspect thrombosis. Definitive diagnosis derives from imaging assessment, with the major role played by grey-scale and Doppler ultrasonography. MR is useful to detect the exact thrombus extension.

The evolution of the ultrasonic features permits to make a stadation of RVT3, and a recent retrospective analysis identified RVT sonographic findings that can predict the renal long-term outcome10. A recent review3 showed that the classic clinical triad including palpable abdominal mass, haematuria and thrombocytopenia, is present in no more than 22% of RVT, suggesting that the presence of only one sign is sufficient to suspect thrombosis.

Thrombolytic therapy is in fact currently recommended only in bilateral RVT1, and it isn’t clear of adverse effects, such as haemorrhagic rupture of the affected kidney and cerebral haemorrhage. In our case we decided to administer heparin because of the thrombus extension in inferior caval vein, in order to reduce the risk of pulmonary and cerebral embolism and we prolonged the therapy for 3 months because of the inherited thrombophilic status. A recent review3 showed that the classic clinical triad including palpable abdominal mass, haematuria and thrombocytopenia, is present in no more than 22% of RVT, suggesting that the presence of only one sign is sufficient to suspect thrombosis. Definitive diagnosis derives from imaging assessment, with the major role played by grey-scale and Doppler ultrasonography. MR is useful to detect the exact thrombus extension.

The evolution of the ultrasonic features permits to make a stadation of RVT3, and a recent retrospective analysis identified RVT sonographic findings that can predict the renal long-term outcome10. As also demonstrated by Winyard et al.7, presenting renal length has a significant association with poor renal outcome; other features associated with renal atrophy seem to be a severely decreased renal perfusion on color Doppler at the diagnosis, subcapsular renal fluid collections, prominent hypoechoic pyramids, patchy echogenicity of renal cortex, renal calcifications and associated adrenal haemorrhage.

In the majority of cases, after an apparent recovery from the acute phase, the evolution is to renal atrophy, with possible development of arterial hypertension and renal failure3. For this reason radionuclide scanning is necessary to monitor renal function during follow up.

Conclusion
Our case confirmed the prominent role that ultrasound scan integrated with Doppler plays in the diagnosis and in the monitoring of neonatal RVT, and its ability to predict the renal long-term outcome. We also observed the utility of heparinic therapy to avoid cerebral and pulmonary embolism from the inferior caval vein; on the other hand we could observe the evolution to renal atrophy despite the therapy, as already indicated in the literature. Lastly, we observed the pathogenic role of Factor V Leiden G1691A mutation in RVT development during neonatal age, as previously demonstrated. Therefore neonatal RVT is a condition that requires molecular investigation to detect this mutation.

References